

## Remarks

### Rejections under 35 U.S.C. § 112

The Examiner has rejected claims 1 – 12 as being indefinite. The Examiner asserts that claim 1 is vague and indefinite in that it is unclear how a promoter that is regulable by a repressor can be considered “constitutive”. In order to more clearly describe the invention claims 1, 2, 3, and 7 have been amended to remove the term “constitutive” and to indicate that transcription from the promoter is active in the absence of a repressor, which is the meaning to be given to the term “constitutive” in light of the specification. The term “constitutive” was used as a convenient means of distinguishing the “constitutive” promoters from, for example, promoters from which transcription is only active in the presence of an inducer or activating agent. As is evident from the specification, the term “constitutive” was not intended to indicate that the “constitutive” promoters are not repressible.

As described on p. 2, lines 16 – 19, the multi-state genetic oscillator of the invention has two alternate expression states. In a first state, transcription from the “constitutive” promoter is active while transcription from the inducible promoter is inactive, while in the second state transcription from the inducible promoter is active while transcription from the “constitutive” promoter is substantially inactive. As further described on p. 3, lines 7 – 23, a first regulatory gene R1 may be expressed from the inducible promoter, and a second regulatory gene R2 may be expressed from the “constitutive” promoter. The product of the first regulatory gene inhibits expression of the second regulatory gene, i.e., it represses expression from the “constitutive” promoter. Thus it is evident that the “constitutive” promoter can be repressed by a repressor (the product of R2). As the foregoing description indicates, the term “constitutive promoter” is used to indicate that transcription from the promoter is active in the absence of a repressor. Applicants submit that replacing the term “constitutive” with its meaning in light of the specification renders the claims definite.

The Examiner has asserted that claim 3 is vague and indefinite in that there is no antecedent basis for the term “second individual promoter”. As suggested by the Examiner, the claim has been amended to read “second inducible promoter”. Applicants thank the Examiner for pointing out this error.

The Examiner has asserted that claim 9 is vague and indefinite in that the metes and bounds of the term "disposed within" are unclear. As suggested by the Examiner, the term "disposed within" has been replaced by the term "comprised within", which is intended to have similar scope.

Claims 2 – 10 are dependent on claim 1 and have been amended to replace the term "switch" with the term "oscillator" as in claim 1, in order to provide proper antecedent basis. It is evident from the specification that the invention may be referred to as a genetic oscillator or a genetic switch. See, e.g., p. 6, lines 25-29, referring to the invention as a multi-state genetic oscillator switch.

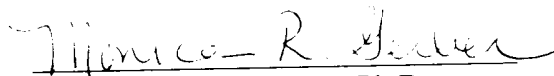
The specification has been amended to refer to co-pending applications by serial number rather than attorney docket number.

In light of the foregoing Amendment and Remarks, Applicants respectfully submit that the present case is in condition for allowance. A Notice to that effect is respectfully requested.

If, at any time, it appears that a phone discussion would be helpful or if questions arise regarding the amendment proposed above, please do not hesitate to contact the undersigned at (617) 248-5071.

Please charge any fees associated with this filing, or apply any credits, to our Deposit Account No. 03-1721.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Monica R. Gerber", written over a horizontal line.

Monica R. Gerber, M.D., Ph.D.  
Registration Number 46,724

Choate, Hall & Stewart  
Exchange Place  
53 State Street  
Boston, MA 02109  
(617) 248-5000  
Dated: August 8, 2003.  
3591581\_1.DOC